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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,475	12/05/2003	Steve Pakola	113476.122US1	3082

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EXAMINER	
KIM, TAEYOON	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/25/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/25/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/729,475	PAKOLA ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-84* is/are pending in the application.

4a) Of the above claim(s) *62, 73-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-61,63-72 and 80-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/14/05;2/22/07; 3/7/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 57-84 are pending.

Election/Restrictions

Applicant's election without traverse of SEQ ID NO:4 in the reply filed on March 30, 2007 is acknowledged. Applicant has previously elected Group I invention and "recombinant microplasmin" as a species with traverse in the reply filed on Oct. 19, 2006. As discussed in the restriction requirement mailed on Jan. 10, 2007, the traverse on the restriction requirement mailed on Oct. 19, 2006 was found not persuasive and the restriction requirement made final. At the same time, new species election has been required in the office action mailed on Jan. 10, 2007. In the reply filed on Feb. 1, 2007, the applicant elected amino acids 543-791 of SEQ ID NO:10. According to the current supplement response, the amino acids 543-791 of SEQ ID NO:10 is further defined as SEQ ID NO:4. After reconsidering the species election requirement requested on Jan. 10, 2007, the examiner has decided to withdraw the species election requirement.

Claims 62 and 73-79 are withdrawn from consideration as being drawn to non-elected subject matter. Claims 57-61, 63-72 and 80-84 have been considered on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 65, 70, 72 and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims (65, 72 and 84) disclose the range of microplasmin being in 0.005 mg to 0.2 mg. It is not clear whether the concentration is based on a unit volume of the composition, total amount per treatment, per eye or a pair of eyes. According to the specification, the concentration appears to be per eye. Applicant is advised to have this limitation in the claims.

Claims 63 and 70 are drawn to the method being performed in the absence of vitrectomy. It is not clear how the method using microplasmin (enzyme, protease) can be performed without vitrectomy. Since the method of using enzyme and/or protease is referred as "pharmacological vitrectomy" (see specification, p.3, lines 20-21), the method using microplasmin is considered as vitrectomy per se.
However, the definition of "vitrectomy" known in the art is a surgery removing some or all of the vitreous humor. It appears that the term "vitrectomy" in the claims points out non-pharmacological vitrectomy. Applicant is advised to amend the claims to clearly point out the subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 57-61, 63-72 and 80-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trese et al. (US 5,304,118; IDS reference) in view of Collen et al. (WO 2002/50290; IDS reference) in further view of Wu et al. (US 4,774,087; IDS reference).

Claims 57-61, 63-69, 71, 72 and 80-84 are drawn to a method of liquefying a vitreous and/or inducing posterior vitreous detachment of an eye of a subject, comprising contacting the vitreous and/or an aqueous humor in the eye with an effective amount of a composition comprising microplasmin (claim 57); a limitation to the microplasmin being recombinant, stabilized, or stabilized and recombinant (claims 58, 67 and 81); a limitation to the composition being a liquid solution and the liquid composition being injected into the vitreous and/or the aqueous humor (claims 59, 68 and 82); a limitation to the subject being a human (claims 60, 69 and 83); a limitation to the method being used for treating a subject having a vitreoretinal disease or disorder (claim 61); a limitation to the method being performed as an adjunct to vitrectomy

(claims 64 and 71); a limitation to the effective amount of microplasmin being in the range of 0.005 mg to 0.2 mg per eye (claims 65, 72 and 84); a method of treating a vitreoretinal disease or disorder of an eye of a subject, comprising contacting a vitreous and/or an aqueous humor in the eye with an effective amount of a composition comprising microplasmin (claim 66); a method of performing a vitrectomy in a subject, comprising contacting a vitreous and/or an aqueous humor in the eye with an effective amount of a composition comprising microplasmin, prior to or at the same time as the removal of the vitreous (claim 80).

Trese et al. teach a method of inducing posterior vitreous detachment in a human eyes and treating certain medical disease and dysfunctions in the eye (column 1, lines 11-14) by injecting one to three units (effective amount) of plasmin during vitrectomy (see Abstract, Figure, and columns 1 and 2). Trese et al. also teach to use the method before surgical vitrectomy or simultaneously with the removal of the vitreous (vitrectomy) (see column 2, lines 26-32).

Trese et al. do not teach the use of microplasmin made recombinantly, stabilized, or stabilized and recombinantly.

Collen et al. teach mammalian plasminogen derivatives such as human microplasmin produced recombinantly and stabilization of such recombinant proteins (see Abstract; p.9, line 24).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace plasmin in the method of Trese et al. with microplasmin of Collen et al.

The skilled artisan would have been motivated to make such a modification because both plasmin and microplasmin share the same enzymatic activity as well known in the art, thus these are considered as art-recognized equivalents.

M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945) (Claims to a printing ink comprising a solvent having the vapor pressure characteristics of butyl carbitol so that the ink would not dry at room temperature but would dry quickly upon heating were held invalid over a reference teaching a printing ink made with a different solvent that was nonvolatile at room temperature but highly volatile when heated in view of an article which taught the desired boiling point and vapor pressure characteristics of a solvent for printing inks and a catalog teaching the boiling point and vapor pressure characteristics of butyl carbitol. "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.)".

Moreover, Wu et al. provide a motivation to use microplasmin over plasmin because of the advantage of the reduced size of microplasmin which does not require complexing and can act directly (see column 3, lines 34-37).

The person of ordinary skill in the art would have had a reasonable expectation of success in using microplasmin in the method of Trese et al. because the activity of microplasmin is well known to be equivalent to plasmin.

Although Trese et al. in view of Collen et al. in further view of Wu et al. do not particularly disclose the range of effective amount of microplasmin being 0.005 mg to 0.2 mg per eye. It would have been obvious for a person of ordinary skill in the art at the time of invention made to optimize the amount of microplasmin for the intended use of vitreolysis. The selection of effective amount of microplasmin would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that identification of the amount of microplasmin sufficient to induce posterior vitreous detachment or vitreolysis is critical to effectively treat the patients. A holding of obviousness over the cited claims is therefore clearly required. The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382.; See also M.P.E.P. § 2144.05

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 57, 63, 66 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trese et al. et al. (supra) in view of Collen et al. (supra) in further view of Wu et al. (supra) and Tanaka et al. (2000; IDS reference AX filed on Jan. 14, 2005).

Claims are drawn to a method of liquefying a vitreous and/or inducing posterior vitreous detachment of an eye of a subject, comprising contacting the vitreous and/or an

aqueous humor in the eye with an effective amount of a composition comprising microplasmin (claim 57); a limitation to the method being performed in the absence of vitrectomy (claims 63 and 70); a method of treating a vitreoretinal disease or disorder of an eye of a subject, comprising contacting a vitreous and/or an aqueous humor in the eye with an effective amount of a composition comprising microplasmin (claim 66).

Trese et al. in view of Collen et al. in further view of Wu et al. renders claims 57 and 66 obvious (see above).

Trese et al. in view of Collen et al. in further view of Wu et al. do not teach that the method of claims 57 and 66 being performed in the absence of subsequent vitrectomy.

Tanaka et al. teach that pharmacological vitrectomy referring to the use of enzymes (e.g. microplasmin) in an effort to liquefy vitreous during or before performing vitreous surgery (vitrectomy). Tanaka et al. further teach the use of plasmin to make the vitreous surgery easier for better outcome or to avoid vitrectomy (see abstract).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use the method of Trese et al. in view of Collen et al. in further view of Wu et al. without additional/subsequent vitrectomy. The skilled artisan would have been motivated to make such a modification because Tanaka et al. teach that the use of pharmacological vitrectomy may allow avoiding subsequent vitrectomy.

The person of ordinary skill in the art would have had a reasonable expectation of success in using the method of Trese et al. in view of Collen et al. in further view of

Wu et al. without further vitrectomy because effective amount of microplasmin would sufficiently achieve posterior vitreous detachment.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 8:00 am - 4:30 pm ET (Mon-Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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